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PATENTS
Attorney Docket No.: BD1 CIP FWC IV

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Sherie L. Morrison, et al.
Serial No.	:	08/266,154
Filed	:	June 27, 1994
For	:	RECEPTORS BY DNA SPLICING AND EXPRESSION
Group Art Unit	:	1806
Examiner	:	Julie E. Reeves, Ph.D.

Palo Alto, California
June 11, 1997

Honorable Assistant Commissioner
of Patents
Washington, D.C. 20231

DECLARATION OF SHERIE L. MORRISON
PURSUANT TO 37 C.F.R. § 1.132

I, SHERIE L. MORRISON, declare that:

1. I am a co-inventor in the above-identified patent application.

2. I have reviewed the May 15, 1996 Declaration of Marc J. Shulman, including its exhibits, that is attached at Tab A.

3. Nothing in that declaration describes our invention in such full, clear, concise, and exact terms as to enable any person skilled in the art to make and use our invention.

4. Specifically, the letter comprising Exhibit A to that declaration identifies the major project of a graduate student working with Dr. Shulman, Gabrielle Boulianne, but contains no detail as to the method used in that project.

5. Exhibit B to that declaration is a copy of a research proposal describing the "desirability of chimeric antibodies." The proposal states:

> "My aim in this project has been to take advantage of the available technology in our laboratory to assay for the expression of functional antibody by chimeric mouse/human immunoglobulin genes. In this way, I can test *whether variable region genes can be transposed to various constant region genes while maintaining functional activity.:...If these constructions produce functional antibody,* this technique could then be applied to generate chimeric antibodies of any antigenic specificity. It will *then* be possible to test *whether* this method provides a general source of specific antibody useful in therapy." (emphasis added.)

The additional disclosure in this proposal does not enable one of skill in the art to practice our invention because it does not contain a full, clear, concise and exact description of co-transfection and co-expression of exogenous antibody chain genes. The two examples in the proposal describe the use of cell lines which produce an endogenous antibody chain which is assembled together with the exogenous chain to form the antibody. While Dr. Shulman states in his declaration that "a method for expressing both genes in the same cell had been developed by Drs. Ochi and Hozumi and communicated to me", the proposal specifically states that this was a "personal communication" and does not describe the method. The proposal contains none of the specifics of vector design or expression sytem.

6. Exhibit C to that declaration constitutes a report sent to the Arthritis Society dated September 1983. One paragraph of that report describes work on chimeric antibodies and in that paragraph Dr. Shulman states:

> "We have begun to test whether the chimeric gene encoding such immunoglobulin can in fact function and whether the antigen binding specificity of the chimeric immunoglobulin is the same as for the original mouse immunoglobulin.... Currently we are testing the function of the chimeric κ gene."

No specifics concerning DNA cloning, vector construction, transfection, or expression systems is given that would enable someone skilled in the art to practice the claimed invention.

7. Exhibit D to that declaration is a copy of an abstract that Dr. Shulman states was published in conjunction with a symposium held from October 2-6, 1983 in Ontario, Canada. That abstract describes what work was done by Dr. Shulman and his colleagues; but it does not explain how the work was done, again omitting specifics concerning DNA cloning, vector construction, and transfection methods that would enable someone skilled in the art to practice the claimed invention.

8. The May 15, 1996 declaration also attaches an earlier declaration and associated exhibits executed by Dr. Shulman on May 21, 1994. Exhibit C to the 1994 declaration constitutes a January 19, 1983 letter from Dr. Shulman to the Johns Hopkins University School of Medicine outlining Dr. Shulman's proposal for the subject matter of his upcoming lecture. Dr. Shulman states:

> "In my presentation I propose to discuss how one might combine the hybridoma system with recombinant DNA and in vitro mutagenesis techniques to generate antibodies where the variable and constant regions are precisely specified. This approach to antibody specificity

> looks good on paper. *My reservations about its feasibility* stem from the facts that (sic) on the one hand our knowledge about V region structure and C region function is rather incomplete, and on the other hand the technical difficulties in altering antibodies are great." (emphasis added.)

9. Dr. Shulman states that Exhibit D to the 1994 declaration constitutes copies of some of the slides which accompanied the lecture discussed in the January 19 letter. Those slides do not enable one skilled in the art to practice the claimed invention for several reasons. First, they do not explain how to clone the exogenous DNA coding for the antibody heavy or light chains or how to assemble that DNA into a functional expression vector. Second, the slide labelled "Construction and Expression of an Ig Heavy Chain Gene" looks similar to textbook diagrams showing normal VDJ assembly and isotype switching. That slide provides no information about how to make the recombinant gene. In addition, there is no slide showing "Construction and Expression", or any other information, specific to the light chain gene. Finally, on the slide labelled "Engineering the V Region", M13 is identified as a possible vector for the immunoglobulin gene. That vector has no eukaryotic selectable markers and therefore is inappropriate for use in a eukaryotic expression system.

10. I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that all these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both under

Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patent issuing thereon.

By [signature]

Sherie L. Morrison

Dated: June 11, 1997

REV. 4/97
For Other Than A Small Entity

Docket No. BD1 CIP FWC IV

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Hon. Assistant Commissioner
for Patents
Washington, D.C. 20231

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TRANSMITTAL LETTER

Sir:

Transmitted herewith: [ ] a Preliminary Amendment; [X] a Response to Examiner's Action; [ ] a Supplemental Amendment; [ ] a substitute Specification; [X] a Declaration; [ ] a Supplemental Declaration; [ ] a Power of Attorney; [ ] an Associate Power of Attorney; [ ] formal drawings; to be filed in the above-identified patent application.

FEE FOR ADDITIONAL CLAIMS

[X] A fee for additional claims is not required.

[ ] A fee for additional claims is required.

The additional fee has been calculated as shown below:

	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA	RATE	ADDITIONAL FEES
TOTAL CLAIMS	30	-	48	* =	0	X $22 =	$0
INDEPENDENT CLAIMS	3	-	6	** =	0	X $80 =	$0
FIRST PRESENTATION OF A MULTIPLE DEPENDENT CLAIM						+ $260 =	$0
						TOTAL	$0

* If less than 20, insert 20.

** If less than 3, insert 3.

[ ] A check in the amount of $_____ in payment of the filing fee is transmitted herewith.

[X] The Commissioner is hereby authorized to charge payment of any additional filing fees required under 37 C.F.R. § 1.16, in connection with the paper(s) transmitted herewith, or credit any overpayment of same, to deposit Account No. 06-1075. A duplicate copy of this transmittal letter is transmitted herewith.

[ ] Please charge $_____ to Deposit Account No. 06-1075 in payment of the filing fee. A duplicate copy of this transmittal letter is transmitted herewith.

EXTENSION FEE

[X] The following extension is applicable to the Response filed herewith; [ ] $110.00 extension fee for response within first month pursuant to 37 C.F.R. § 1.17(a); [ ] $390.00 extension fee for response within second month pursuant to 37 C.F.R. § 1.17(b); [X] $930.00 extension fee for response within third month pursuant to 37 C.F.R. § 1.17(c); [ ] $1,470.00 extension fee for response within fourth month pursuant to 37 C.F.R. § 1.17(d).

[X] A check in the amount of [ ] $110.00; [ ] $390.00; [X] $930.00; [ ] $1,470.00; in payment of the extension fee is transmitted herewith.

[X] The Commissioner is hereby authorized to charge payment of any additional fees required under 37 C.F.R. § 1.17 in connection with the paper(s) transmitted herewith, or to credit any overpayment of same, to Deposit Account No. 06-1075. A duplicate copy of this transmittal letter is transmitted herewith.

[ ] Please charge the [ ] $110.00; [ ] $390.00; [ ] $930.00; [ ] $1,470.00; extension fee to Deposit Account No. 06-1075. A duplicate copy of this transmittal letter is transmitted herewith.

Vicki S. Veenker

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I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231,

on June 11, 1997

Vicki S. Veenker

Name of Person Signing Certificate

Vicki S. Veenker

Signature of Person Signing Certificate

June 11, 1997

Date of Signature